



Europäisches Patentamt
European Patent Office
Office européen des brevets

⑪ Publication number:

0 258 749

A2

⑩

EUROPEAN PATENT APPLICATION

⑫

Application number: 87112087.9

⑬

Int. Cl.4: A61L 17/00

⑭

Date of filing: 20.08.87

⑮

Priority: 05.09.86 US 903799
05.09.86 US 903791
05.09.86 US 903798

⑯

Date of publication of application:
09.03.88 Bulletin 88/10

⑰

Designated Contracting States:
AT BE CH DE ES FR GB GR IT LI LU NL SE

⑲

Applicant: AMERICAN CYANAMID COMPANY
1937 West Main Street P.O. Box 60
Stamford Connecticut 06904-0060(US)

⑳

Inventor: Lehmann, Leonard Theodore
45 Aunt Hack Road
Danbury Connecticut 06811(US)
Inventor: Wang, David Wei
800 Overbrook Drive
Vestal New York 13850(US)
Inventor: Casey, Donald James
9 Revere Place
Ridgefield Connecticut 06877(US)
Inventor: Rosati, Louis
182 Sunrise Hill Road
Norwalk Connecticut(US)
Inventor: Jarrett, Peter Kendrick
American Cyanamid Company 1937 West
Main Street
Stamford Connecticut 06904(US)

㉑

Representative: Wächtershäuser, Günter, Dr.
Tal 29
D-8000 München 2(DE)

㉒

Surgical filament coating.

㉓

Surgical filament coatings are disclosed. The filament can be a suture or ligature. The coating can be calcium stearoyl-2-lactylate, a diblock or a triblock copolymer, or a random copolymer having a glycolic acid ester and trimethylene carbonate linkages.

EP 0 258 749 A2

SURGICAL FILAMENT COATINGS

This invention relates to the use of degradable thermoclastic hydrogels consisting of block polymers as a coating and lubricating finish for surgical articles including sutures and ligatures. These materials will impart lubricity to, and improve the tie-down properties of a multifilament absorbable suture or ligature in both wet and dry state. The suture or ligature can be manufactured from a homopolymer (e.g., DexonTM, American Cyanamid Co., NJ, USA) or copolymer (e.g., VicrylTM, Ethicon, Inc., NJ, USA) of glycolic acid. In addition, these materials are capable of being completely degraded and eliminated from the body over a period of time. A particular advantage of these materials is their thermoplastic nature, that is, they can be applied to sutures by conventional solution or thermal techniques.

Recently, there has been interest in using hydrogels in a wide variety of biomedical applications such as contact lenses, burn dressings, blood and tissue compatible implants, lubricant coatings for surgical implants, and drug delivery devices. In some of these areas, crosslinked hydrogel materials have met with great success. However, these materials suffer drawbacks, such as a lack of processibility, which are a consequence of their crosslinked nature.

Our approach to this problem was to investigate the use of block copolymers as thermoplastic biodegradable hydrogels for suture coating applications. In an ABA triblock example of these block polymers, the middle (B) block is a water soluble polymer such as a poly(alkylene oxide) and the end blocks (A) are comprised of degradable random copolymers of glycolide (Gly) and trimethylene carbonate (TMC). The middle and end blocks of this block copolymer are chemically incompatible and the result is a phase separated system with poly(alkylene oxide) regions dispersed throughout the Gly/TMC matrix. When exposed to an aqueous environment, the block polymer picks up an amount of water which is a function of the composition and molecular weight of the various block structures. The thermoplastic nature of the block polymers allows for lubricant coatings to be applied by known solution or melt processes. The crystalline poly(alkylene oxide) segments serve, in the dry state, as temperature dependent crosslinks which hold the coating securely in place and minimize coating flow on storage of the surgical suture.

The method of choice for preparing the above block copolymers is the melt ring-opening copolymerization of glycolide and trimethylene carbonate using specially purified, commercially available difunctional or monofunctional poly(alkylene glycols) as initiators. These polymerizations are conducted in a stirred reactor at about 165°C under nitrogen. When maximum melt viscosity has been reached, the polymer is discharged and allowed to cool to room temperature. Oligomeric material can be removed by reprecipitation from methylene chloride solutions into methanol or ethanol.

Samples of the above polymers are extruded at 60-100°C with an extruder to yield fibers of 1.5 mm average diameter. The fibers are then cut into 1" lengths and several are placed in deionized water at room temperature. At various time intervals, the fibers are withdrawn, wiped thoroughly to remove any surface liquid, and the water uptake is measured gravimetrically. Alternatively, the uptake can be measured from thin films (0.6 mm) prepared by compression molding the polymer at 90°C, or by casting thin films of the polymer from solution.

The Above embodiments are more fully described in the following examples.

40

Example 1

Purification of Materials

45 DL-lactide: DL-lactide was purchased from Purac, Inc. One kilogram of DL-lactide is refluxed for 1 1/2 hours with toluene (1500 g) which has been dried by distillation from benzophenone ketyl. The residual water is removed from the DL-lactide by collection of the toluene/water azeotrope in a Dean-Stark trap. The dry DL-lactide solution is allowed to cool to room temperature and placed in the refrigerator overnight. The crystallized DL-lactide is then quickly filtered and dried in a vacuum oven at room temperature. Recrystallization yield is 84%.

Polyethylene Glycol-8,000: Polyethylene glycol-8,000 (PEG 8,000) (160 g) is dissolved in methanol (1600 ml). The PEG solution is then freed of catalyst impurities and deionized by slowly passing the solution through a methanol conditioned indicating mixed bed anionic and cationic ion-exchange resin (Amberlite MB-3, Rohm and Haas Company, PA, U.S.A.). After elution from the column, the PEG is crystallized by placing the solution in a freezer overnight. The crystalline PEG is then filtered and air dried

for 2 hours. The PEG is further purified by recrystallization from acetone (1600 ml). The recrystallized PEG is filtered and dried in a vacuum oven at room temperature overnight. Prior to polymerization, the desired amount of purified PEG is dried further by heating in a vacuum oven at 70°C with P_2O_5 as a desiccant. PEG-14,000 and PEG-20,000 are purified in the same way.

5 Pluronic F68: Pluronic F68 was purified by the same technique as described for PEG above but without the acetone recrystallization step. The methanol recrystallized Pluronic F68 was filtered and dried in a vacuum oven at room temperature. Prior to polymerization, the Pluronic F68 was further dried by heating in a vacuum oven at 70°C with P_2O_5 as a desiccant.

10 Pluronic P105: Pluronic P105 purified by the same method described for PEG above. The polymer was recovered from the methanol solution using a rotary evaporator. Residual methanol was removed by drying in vacuum to constant weight. The material was not recrystallized from acetone. Prior to polymerization the Pluronic P105 was dried further by heating in a vacuum oven at 50°C with P_2O_5 as a desiccant.

Polyethylene Glycol Methyl Ether: Polyethylene glycol methyl ether, nominal molecular weight 5000, was purified in the same way as described for PEG above.

15

Example 2

Synthesis of (Gly/TMC)-(PEO 14,000)-(Gly/TMC) ABA Triblock Copolymer (Gly/PEO/TMC: 34/41/25)

20

A 250 ml flask is charged with PEG-14000 (50 g, 0.0036 mole). The flask is placed in a vacuum oven and the PEG is dried overnight under vacuum at 70°C with P_2O_5 as a drying agent. The flask is then placed in a glove bag under N_2 . Glycolide (25.0 g, 0.21 mole) and trimethylene carbonate (25.0 g, 0.24 mole) are charged to the flask and the contents are melted and mixed under N_2 . The monomer mixture is then quickly transferred into a stirred reactor which has been heated under a nitrogen flow to 165°C. Stannous octoate (0.16 ml, 4.9×10^{-4} mole) is then quickly charged to the reactor with the use of a syringe. The polymer melt is stirred at 40 rpm for approximately 3 hours at 165°C. This time period corresponds to a maximum in the melt viscosity. The polymer is discharged from the reactor and allowed to cool to room temperature. A portion of the crude polymer (42.8 g) is dissolved in CH_2Cl_2 (250 ml) and reprecipitated dropwise into rapidly stirred absolute ethanol (3000 ml). After filtration and drying to constant weight, the reprecipitation yield was determined to be 98%. The inherent viscosity of the polymer (0.5g/dL, in $CHCl_3$ at 30°C) was 0.38 dL/g. The composition was analyzed by 1H -NMR and was found to be 34/41/25 weight percent Gly/PEO/TMC. The Tg of the polymer was 11°C, the melting point (Tm) was 59°C.

35

Examples 3-14

Several polymers were prepared as in Example 2 with varying PEG contents and PEG molecular weights (Table I). In many of the Gly/PEO/TMC triblock copolymers, the charged ratio of Gly/TMC is 60/40 weight percent. This allows for maximum Tg of the rubbery end blocks (9°C) while still maintaining solubility in common organic solvents. Differential scanning calorimetry (DSC) clearly shows phase separation in these materials. The Tg of the rubbery end blocks (7-16°C) is very close to the Tg of a 60/40 random Gly/TMC polymer. In addition, the Tm of the crystalline PEO segments are only lowered 5-10°C.

45

Example 15

Synthesis of (Gly/TMC)-(PEO-8000)-(Gly/TMC) ABA, (Gly/PEO/TMC: 59/8/35)

50

Glycolide (117.0 g, 1.01 mole), trimethylene carbonate (71.0 g, 0.70 mole), PEG-8000 (12.0 g) and stannous octoate (0.33 ml, 1.0×10^{-3} mole) were combined in a stirred reactor as in Example 2. The reaction mixture was then stirred at 169°C and 36-40 rpm for 1.5 hours. The polymer was recovered as in Example 2. The properties of this polymer are summarized in Table I.

55

Example 16:

Synthesis of (Gly/TMC)-(PEO-8000)-(Gly/TMC) ABA, (Gly/PEO/TMC: 54/8/38)

- 5 Glycolide (110.4 g, 0.95 moles), trimethylene carbonate (73.6 g, 0.72 moles), PEG-8000 (16.0 g) and
stannous octoate (0.32 ml, 9.96×10^{-4} moles) were combined and allowed to polymerize as in Example 15.
The properties of this polymer are summarized in Table I.

10 Example 17

Synthesis of (Gly/TMC)-(PEO-8000)-(Gly/TMC) ABA, (Gly/PEO/TMC: 54/10/36)

- 15 Glycolide (108.0 g; 0.93 moles), trimethylene carbonate (72.0 g, 0.71 moles), PEG-8000 (20.0 g) and
stannous octoate (0.32 ml, 9.96×10^{-4} moles) were combined and allowed to polymerize as in Example 15.
The properties of this material are summarized in Table I.

20

25

30

35

40

45

50

55

5
10
15
20
25
30
35
40
45
50
55

TABLE I
Glycolide/PEO/TMC Polymers

<u>Example</u>	<u>Charged Composition (Gly/PEO/TMC Wgt. %)</u>	<u>PEG MW</u>	<u>η in h (Solvent)</u>		<u>Gly/PEO/TMC Composition by H-NMR (wt %) As Polymerized</u>	<u>Tg (°C) As Reprecipitated</u>	<u>Tm (°C)</u>
			<u>As Polymerized</u>	<u>Reprecipitated</u>			
3	25/50/25	14,000	---	0.40 (CHCl ₃)	---	30/43/27	--
4	32/50/18	14,000	---	0.45 (CH ₂ Cl ₂)	---	31/54/15	--
5	48/20/32	14,000	---	0.45 (CHCl ₃)	---	49/19/32	16 57
6	54/10/36	14,000	---	0.34 (CH ₂ Cl ₂)	---	55/11/34	12 54
7	42/30/28	14,000	0.45 (CH ₂ Cl ₂)	0.45 (CH ₂ Cl ₂)	---	44/29/27	15 58
8	42/30/28	8,000	0.40 (CH ₂ Cl ₂)	0.38 (CH ₂ Cl ₂)	---	43/31/26	16 55
9	48/20/32	8,000	0.42 (CH ₂ Cl ₂)	---	48/21/31	---	14 55
10	54/10/36	8,000	0.46 (CH ₂ Cl ₂)	0.33 (CHCl ₃)	50/10/40	50/8/42	10 53
11	54/10/36	20,000	---	---	---	---	7 47
12	48/20/32	20,000	---	---	---	6	52
13	42/30/28	20,000	---	---	---	11	54
14	57/5/38	8,000	0.41 (CHCl ₃)	0.38 (CHCl ₃)	57/5/38	58/5/37	--
15	58/6/36	8,000	0.42 (CHCl ₃)	0.40 (CHCl ₃)	59/6/35	59/6/35	--
16	55/8/37	8,000	0.44 (CHCl ₃)	0.42 (CHCl ₃)	53/8/39	54/8/38	--
17	54/10/36	8,000	0.45 (CHCl ₃)	0.40 (CHCl ₃)	54/10/36	54/10/36	--

Example 18

5

Synthesis of (Gly/dL-Lact)-(PEO-8000)-(Gly/dL-Lact) ABA, (Gly/dL-Lact/PEO: 36/54/10)

Glycolide (54.0 g, 0.46 moles), dL-lactide (81.0 g, 0.56 moles), PEG-8000 (15.0 g) and stannous octoate (0.32 ml, 9.96×10^{-4} moles) were combined and allowed to polymerize as in Example 2. The properties of this polymer are summarized in Table II>

Example 19

15

Synthesis of (Gly/L-Lact)-(PEO-8000)-(Gly/L-Lact) ABA: (Gly/L-Lact/PEO: 27/65/8)

Glycolide (53.2 g, 0.46 moles), L-lactide (130.8 g, 0.91 moles), PEG-8000 (16.0 g) and stannous octoate (0.05 ml, 1.56×10^{-4} moles) are combined and allowed to polymerize by the procedure described in Example 15. The properties of this polymer are summarized in Table II>

20

Example 20

25

Synthesis of (L-Lact/TMC)-(PEO-8000)-(L-Lact/TMC) ABA, (L-Lact/TMC/PEO: 43/49/8)

L-lactide (88.0 g, 0.61 moles), trimethylene carbonate (96.0 g, 0.94 moles), PEG-8000 (16.0 g) and stannous octoate (0.31 ml, 9.74×10^{-4} moles) are combined and allowed to polymerize by the procedure described in Example 15. The properties of this polymer are summarized in Table II.

30

Example 21Synthesis of (Gly/dL-Lact)-(PEO-20,000)-(Gly/dL-Lact) ABA, (Gly/dL-Lact/PEO: 21/25/54)

35

dL-lactide (25.0 g, 0.17 moles), glycolide (25.0 g, 0.21 moles), PEG 20,000 (50.0 g) and stannous octoate (0.16 ml, 4.94×10^{-4} moles) are combined and allowed to polymerize by the procedure described in Example 2. The properties of this polymer are described in Table II.

40

45

50

55

5
10
15
20
25
30
35
40
45
50
55

Table II
Terpolymers With PEO Midblocks and Various Endblocks

Example	Charged Composition	η_{inh} (Solvent)			Composition by 1H -NMR (wt%)		
		PEG MW	As Polymerized	Reprecipitated	Polymerized	Reprecipitated	Tg Tm
18	Gly/dl-lactide/ PEO: 36/54/10	8,000	0.49(CHCl ₃)	0.35(CHCl ₃)	36/54/10	36/54/10	--- ---
19	Gly/l-lactide/ PEO: 27/65/8	8,000	0.73(CHCl ₃)	-----	27/65/8	-----	36 ---
20	l-Lactide/TMC/ PEO: 44/48/8	8,000	0.56(CHCl ₃)	-----	43/49/8	-----	0 ---
21	Gly/dl-lactide/ PEO: 25/25/50	20,000	-----	0.43(CHCl ₃)	-----	21/25/54	42 57

Example 22

5

Swelling Behaviour of Examples 3, 4 and 21

A film was prepared by solution casting a 20% w/v solution of the polymer of Example 3 in CH₂Cl₂. After the solvent had evaporated overnight, the film was dried further under vacuum at room temperature overnight. Films made from the polymers of Example 3, 4 and 21 were placed in water at 37°C with stirring. After 24 hours, films from Example 3 and Example 4 had formed emulsions. By day 3, the film from Example 21 had also formed an emulsion.

15 Example 23Swelling Behaviour of Example 7 (Gly/PEO/TMC: 44/29/27)

A sample of the polymer from Example 7 (1.5 g) was extruded at 110°C to yield a 1.5 mm diameter fiber. From the fiber 5 samples, lengths each approximately 1" were cut. The samples were placed in deionized water at room temperature. Periodically, the samples were withdrawn, wiped dry, and the water uptake measured gravimetrically. The water uptake is shown in Table III. From the values at 1280 min., the equilibrium water uptake for fibers was calculated to be 232 ± 3%.

Water uptake analysis was performed on 4 samples of films of the polymer of Example 7 (12 x 4 x 0.6 mm). The results are shown in Table III. The shorter time to reach an equilibrium value of water uptake in the films is attributable to the greater surface-to-volume ratio in the films.

30

35

40

45

50

55

Table III

Water Uptake by Fibers and Films of 44/29/27
Gly/PEO/TMC (Ex. 7)

	<u>Fibers</u>		<u>Films</u>	
	Time (min)	% H ₂ O ^A Uptake	Time (min)	% H ₂ O ^A Uptake
15	5	31.1	5	136.7
	18	60.9	22	238.7
20	32	89.3	35	271.0
	45	107.9	63	279.5
	65	133.6	81	282.2
25	90	158.2	216	279.1
	118	183.7	363	253.5
30	148	204.3	1560	266.3
	179	223.3		
	1155	237.6		
35	1280	235.5		

$$A = \frac{(\text{Wt Swollen} - \text{Wt Dry})}{\text{Wt Dry}} \times 100$$

Example 24Swelling of Various Hydrogels

Water uptake experiments were carried out on fibers of several Gly/PEO/TMC hydrogels and one Gly/dL-Lactide/PEO hydrogel (Table IV). Measurements were carried out at room temperature in deionized water. All reported equilibrium uptake values are averages of 4 or 5 samples.

TABLE IV
Combined Swelling Data on Polymers

<u>Example</u>	<u>Polymer</u>	<u>PEG MW</u>	<u>PEO Content (Wgt. %)</u>	<u>% H₂O Uptake</u>	<u>T_{eq}</u>
14	GLY/PEO/TMC	8,000	5	27.9 + 5.4 1,3	~13 days
10	GLY/PEO/TMC	8,000	8	124.1 + 7.4 1,3	~1 day
10	GLY/PEO/TMC	8,000	10	11.3 + 0.9 1,2	4
18	GLY/dl-lactide/PEO	8,000	10	9.9 + 1.3 1,3,5	5
9	GLY/PEO/TMC	8,000	21	163.0 + 1.8 1,2	4
8	GLY/PEO/TMC	8,000	31	224.5 + 15.1 1,3	4
6	GLY/PEO/TMC	14,000	11	125.8 + 4.5 1,3	4
5	GLY/PEO/TMC	14,000	19	164.9 + 11.1 1,3	4
7	GLY/PEO/TMC	14,000	29	235.9 + 3.1 1,3	~17 hrs.
7	GLY/PEO/TMC	14,000	29	260.8 + 10.3 1,6	20 min.
11	GLY/PEO/TMC	20,000	10	61.0 + 0.5 1,2	4
12	GLY/PEO/TMC	20,000	20	169.0 + 0.8 1,2	4
13	GLY/PEO/TMC	20,000	30	289.2 + 5.6 1,2	4

1 = fiber (dimensions = 10 mm x 1.5 mm diameter)

2 = as polymerized

3 = reprecipitated

4 = not determined

5 = not at equilibrium by day 13

6 = film (dimensions = 12 x 4 x 0.6 mm)

Several generalizations about the data in Table IV can be made. The time to reach an equilibrium value of water uptake depends on the shape of the sample (Example 7 fiber vs. film). It would also appear that the time to reach an equilibrium value of water uptake decreases as the PEO content increases.

- 5 Within the scatter in the data, equilibrium water uptake is linearly related to the PEO content in the range 5-30%. There is no noticeable effect of the MW of the PEO block on the swelling of these triblock polymers (within the range of PEO MW 8,000-20,000).

One important difference noted in Table IV is the contrast of Example 10 (Gly/PEO/TMC) with Example 18. (Gly/PEO/dL-Lactide): Both have approximately the same percent of PEO 8,000; however, a reprecipitated sample of Example 10 had an equilibrium water content of 124% (T_{eq} 1 day) vs. 9.9% by day 13 for a reprecipitated sample of Example 18. The difference can be rationalized by looking at the differences of the two matrices. In the case of the sample of Example 10 the Gly/TMC matrix is free to deform to accommodate the dimensional changes caused by the swelling. With the sample of Example 18, however, the Gly/dL-Lactide matrix has a dry T_g of approximately 30°C. At room temperature, it is in a glassy state and cannot deform as easily to accommodate the dimensional changes necessary to swell. This should result in a slower water uptake curve (note that at 13 days equilibrium has not been reached) until the Gly/dL-Lactide matrix is sufficiently plasticized by water.

20 Example 25

Suture Coating Experiments

Two methods are used to apply the coating polymer to an uncoated 1/0 polyglycolic acid braided suture. In the hand dip method, which is largely used to screen potential coating candidates, the braided strand is run under an inverted "U" guide mounted on a holder immersed in a solution of the coating polymer. Any solvent can be used that will dissolve the coating polymer and not damage the PGA braid. Typically, methylene chloride, chloroform, 1,1,1-trichloroethane, or acetone can be used as solvents. After each pass through the solution, the coated sutures are air dried in a hood. Several passes can be made through the solution to increase the amount of material picked-up on the braid. After the final pass, the braid is dried at room temperature and reduced pressure for 2-4 hours.

The preferred method of coating uses a pump to supply coating solution to a ceramic guide through which the PGA braid is passed at a controlled state. The coated braid is then passed through a hot air oven to remove the coating solvent. This braid is cut, needled, sterilized, vacuum dried and packaged.

35 A general description for the coating of a surgical suture is as follows. A commercially available coater (e.g. from the Bouligny Co., U.S.A.) is set to operate on a filament traveling at a speed of 50 feet per minute. The circulating air in the drying oven is adjusted to be 80°C.

There is only one pass of the filament through the capillary coating apparatus, and then through the drying oven. The coating pump is adjusted to give about 5 to 8 drops per minute at the capillary apparatus.

40 Using the above coating method, the percent pickup is about 3.5 to 3.6 percent based on the weight of the filament. It is to be understood that this amount of pickup can be increased or decreased by a person skilled in the art without undue experimentation by adjusting the above parameters. Preferably, the amount of pickup is increased by decreasing the amount of solvent in the coating formulation, and vice versa.

The dip-coated braid and the machine coated braid are easily tested for improvements provided by the coating to both knot repositioning and knot security. Size 1/0 PGA braid samples were coated with several Gly/PEO/TMC terpolymers (Table V) and with three lactide based terpolymers (Table VI).

TABLE V
In Vitro Coating Performance: GLY/PEO/TMC Terpolymers

		<u>Pick-up (g)</u> <u>(wt%)</u>	<u>Knot</u> <u>Repositioning (mm)</u> (2)	<u>Knot</u> <u>Security (mm)</u> (3)	<u>Knot Run Down (4)</u>	
<u>Coating Polymer</u>	<u>No Coating</u>				<u>Wet</u>	<u>Dry</u>
Control	No Coating	0	2.8	1.6	--	--
Ex. 5	GLY/PEO/TMC: 49/19/32	0.4	22.4	10.0	RW	RW
Ex. 14	GLY/PEO/TMC: 58/5/37	0.3	3.0	2.0	L	--
Ex. 15	GLY/PEO/TMC: 59/6/35	0.9 1.8 2.6	15.0 19.6 18.8	5.1 7.8 4.9	L RC RC	RD RC RC
Ex. 16	GLY/PEO/TMC: 54/8/38	1.1 1.9 2.7	27.7 28.0 28.2	9.7 12.8 14.4	RC RW RW	RW RW RW
Ex. 17	GLY/PEO/TMC: 54/10/36	0.9 1.8 2.3	27.9 27.7 27.7	8.2 7.5 6.7	RC RC RW	RW RW RW

TABLE V FOOTNOTES

- 5 (1) The coatings were applied to 1/0 polyglycolic acid braid from a 2% (wt/vol.) solution of the coating material dissolved in methylene chloride.
- 10 (2) This test measures the ability of a suture to be snugged in. A loop is passed around a steel rod and tied with a square knot. The knot is set to a prescribed tension with an Instron tester, and the tension is then removed. After resetting the gage length, the loop is tested to break. The breaking strength of the loop and elongation-to-break are recorded. The material elongation at the point of knot break is determined separately in a straight pull test, and subtracted from the knot breaking elongation to obtain the slippage in mm within the knot up to the breaking point. Samples were tested immediately after 30 seconds immersion in saline solution (0.9% NaCl in distilled water).
- 15 (3) The tensions used to set the knots and all the other conditions of knot tying and testing, are practical laboratory conditions, but may not correspond to actual surgical practice. The knot snug in may not correlate with clinical experience.
- 20 (3) A strand is tied to itself to form a loop, the knot is set to a prescribed tension, the loop is cut, and the cut ends are clamped in the jaws of an Instron tester. The breaking strength and elongation-to-break are measured. The maximum slippage is recorded for the knots that break. This is defined as the difference between the average elongation-to-break of the knotted suture and the average elongation of an unknotted strand, measured at a load equal to the knot breaking strength. Samples are tested immediately after 30 seconds immersion in saline solution.
- 25 (4) Square knots were formed in hand-dipped 1/0 polyglycolic acid braid using a conventional suture tying board. The knot was then run down to the board to assess the stick-slipping of the knot (chatter) as it runs down and to assess the force required to initiate and sustain the run-down. The abbreviations are: L, Lock; RC, Runs with Chatter; RD, Runs with Difficulty; RW, Runs Well. The comparisons are made on dry suture and on suture wet with saline.

30

TABLE VIIn Vitro Coating Performance: Terpolymers
Made With Lactide

	<u>Coating Polymer</u>	<u>(Wt %)</u>	<u>Knot Run Down⁽¹⁾</u>	
			<u>Wet</u>	<u>Dry</u>
40	Ex. 19 Gly/l-Lactide/ PEO: 27/65/8	1-3	L	L
45	Ex. 20 l-Lactide/TMC/ PEO: 43/49/8	1-3	L	L
50	Ex. 21 Gly/dL-Lactide/ PEO: 21/25/54	1-3	RW	RW

55 (1) L: Locks; RW: Runs Well

From the in vitro data on knot repositioning with these coated braids, it is evident the Gly/PEO/TMC coatings with PEO contents as low as 6% permit easy movement of a square knot, whereas lactide based terpolymer coatings locked rather than reposition if the PEO content was low (~8%). However, if the PEO content was high in the lactide based terpolymer, the coating allowed for good repositioning, indicating that the minimum acceptable PEO content is dependent upon the end block composition.

Example 26

A Gly/PEO/TMC 59/6/35 weight % polymer from Example 15 was dissolved in methylene chloride to give a 2% solids solution. A size 1/0 uncoated Dexon braid was immersed in this solution and dried. Multiple immersions were made so that different percent pick-up levels were obtained. A sample having 0.9% pick-up (based on the weight of the fiber) was later needled with a tapered needle, wound, packaged and sterilized using standard ethylene oxide sterilizing techniques. A surgeon used eight of these coated sutures to close a midline incision of a male dog, while evaluating the knot repositioning and the immediate knot security of these sutures.

Example 27

Same as Example 26 except the polymer used was Gly/PEO/TMC 54/8/38 from Example 16.

Example 28

Same as Example 26 except the polymer used was Gly/PEO/TMC 54/10/36 from Example 17.

Example 29

Synthesis of (Gly/TMC) [Pluronic F68] (Gly/TMC) ABA (Gly/Pluronic F68/TMC: 56/8/36 PentaBlock Copolymer

Pluronic F68 (BASF Wyandotte, U.S.A.) is a triblock copolymer of poly(ethylene oxide) (PEO) (80 mole %) and poly(propylene oxide) (PPO) (20 mole %) where PPO forms the middle block and the total molecular weight is about 8400. Like PEO, this copolymer is terminated with hydroxyl groups which can be used as an initiator for the ring opening polymerization of cyclic esters.

Glycolide (82.8 g), trimethylene carbonate (55.2g), Pluronic F68 (12.0 g) and stannous octoate (0.242 ml), were combined in a stirred reactor as in Example 2. The reaction mixture was then stirred at 165°C and 40 rpm for 1.5 hours. The polymer was recovered as in Example 2, and then characterized as follows: η_{inh} (CHCl₃): 0.40; Composition: 56/8/36 (¹H NMR); tg:14°C; Tm 42°C.

Table VII summarizes the in vivo ratings for 1/0 polyglycolic acid braid coated with the Gly/PEO/TMC block polymers, or with the block polymer containing a Pluronic F68 midblock of Examples 26 to 29.

45

50

55

TABLE VII
In Vivo Coating Evaluations (1)

<u>Coating Polymer</u>	<u>Pick-Up (wt %) (2)</u>	<u>Knot Repositioning Ability (3)</u>	<u>Knot Security square</u>	<u>Knot Security square + 2</u>
Control	No Coating	0	0/8	4/4
Ex. 26	Gly/PEO/TMC: 59/6/35	0.9	5/8	4/4
Ex. 27	Gly/PEO/TMC: 54/8/38	1.1	7/8	4/4
Ex. 28	Gly/PEO/TMC: 54/10/36	1.8	8/8	1/4
Ex. 29	Gly/F-68/TMC: 56/8/36	2.3	17/18	--
				17/17

TABLE VII FOOTNOTES

5

(1) Coated, needle, and sterilized sutures were tested in dogs.

(2) The coatings were applied to 1/0 polyglycolic acid braid from a 2% (wt/vol) solution of the coating material dissolved in methylene chloride.

10

3. A suture coated with the test material is passed through two sides of a wound in the animal. A square knot is formed in the suture approximately 12-15 mm from the final knot position required to close the wound. The two ends of the suture are then pulled to slide the knot into position. Knots that slide properly are rated 1 while knots that fail to move into position are rated 0. The rating for a coating is the sum of the "I" ratings divided by the total number of test specimens.

15

(4) Immediate knot security is determined by using a pair of curved tweezers to tug at the 8 to 10 mm length of the ears of a square knot or a square knot with two additional throws. Knots that are secure are rated 1 while knots that can be loosened are rated 0. The rating for a coating is the sum of the "I" ratings divided by the total number of test specimens.

20 Example 30Synthesis of (Gly/TMC) [Pluronic P105] (Gly/TMC) ABA (Gly/Pluronic P105/TMC: 56/9/35 PentaBlock Copolymer

25

Pluronic P105 (BASF Wyandotte) is a triblock copolymer of poly(ethylene oxide) (PEO) (50 mole %) and poly(propylene oxide) (PPO) (50 mole %) where PPO forms the middle block and the total molecular weight is about 6500. Like PEO, this copolymer is terminated with hydroxyl groups which can be used as an initiator for the ring opening polymerization of a cyclic ester.

30

Glycolide (54 g), trimethylene carbonate (36 g) Pluronic P105 (10.0 g) and stannous octoate (0.19 ml), were combined in a stirred reactor as in Example 2. The reaction mixture was then stirred at 165°C and 40 rpm for 1.5 hours. The polymer was recovered as in Example 2, and then characterized as follows: η_{inh} (CHCl₃): 0.35; Composition: 56/9/35 (¹H NMR).

A 1/0 polyglycolic acid braid was coated with 1 to 3% of this polymer. In in vitro knot-run-down tests with these coated sutures, square knots were found to run down well both wet and dry.

35

Example 31Synthesis of (PEO)-(Gly/TMC) AB (Gly/PEO/TMC: 57/6/37) Diblock Copolymer

40

Poly(ethylene glycol) methyl ether (PEO-5000) was purchased from Aldrich Chemical Company. The molecular weight was reported to be 5000. This polymer is terminated by one hydroxyl group and one methyl ether group. Only one end of this molecule, therefore, can be used to initiate the ring opening polymerization of cyclic esters, forming an AB diblock copolymer.

45

Glycolide (84.6 g), trimethylene carbonate (54.4 g) PEO 5000 (10.0 g) and stannous octoate (0.242 ml), were combined in a stirred reactor as in Example 2. The reaction mixture was then stirred at 165°C and 40 rpm for 1.5 hours. The polymer was recovered as in Example 2, and then characterized as follows: η_{inh} (CHCl₃): 0.42; Composition: 57/6/37 (¹H NMR); tg: 12°C Tm: 59°C.

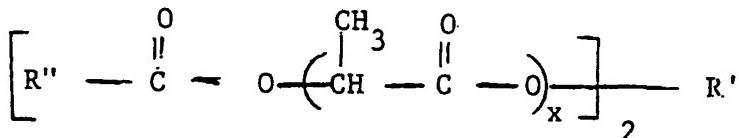
50

A 1/0 polyglycolic acid braid was coated with 1 to 3% of the polymer. In in vitro knot-run-down tests with these coated sutures, square knots were found to run down well both wet and dry.

II

Another coating composition of this invention comprises a compound of the formula:

55



wherein x is at least 2, R' is selected from the group consisting of an alkaline-earth metal ion or radical, and R' is an alkyl group having at least 6 carbon atoms in the backbone. An ester of R' having from about 12 to 22 carbon atoms, and mixtures thereof, are preferred.

A compound of this formula can be prepared by methods known in the prior art. Illustrative of prepared compounds are magnesium, barium, aluminum or zinc palmityl lactylate; and calcium, magnesium, barium, aluminum or zinc oleyl lactylate. Particularly preferred is a commercially available food grade of calcium stearoyl-2-lactylate.

Illustrative of solvents useful in preparing the calcium stearoyl-2-lactylate coating composition are the aromatic series of benzene, toluene, xylene and mesitylene, and the aliphatic solvents, 1,1,2-trichloroethane and chloroform.

A fatty acid ester coating composition of the above formula is conveniently applied to a suture by passing the suture through a container of the coating composition. Other conventional methods of applying coatings or finishes to continuous strands of fibers may also be used with substantially similar results, e.g. melt coating. Preferably, the application of the coating to the suture is regulated to provide from about 1 to 15 percent dry coating by weight of the suture fiber.

The coating adheres well to the suture. Also, the coating is translucent so that the appearance of the coated suture is not significantly altered by the coating. Also, there is no appreciable dusting or flaking of the coating during suture tie-down.

In coating multifilament sutures with the fatty acid ester in accordance with the present invention, it is not necessary that every filament within the suture be individually or completely coated. Under most circumstances, the coating will penetrate at least partially into the interstices of the suture. What is critical is that the outer surface of the suture be well coated in order to reduce frictional forces during suture tie-down.

The amount of coating composition applied to the suture fiber, or the coating add-on, will vary depending upon the construction of the fiber. For example, the number of filaments and tightness of a braid or twist, and the nature of the coating material, e.g., its viscosity and consistency will vary the amount of coating applied to the fiber.

In general, the dry coating composition applied to a braid will constitute from about 1 to 5 percent by weight of the coated suture fiber. However, it is to be understood that coating composition add-on may range from as little as about 0.5 percent by weight to as much as about 10 percent by weight or higher in some cases.

As a practical matter, and for reasons of economy and general performance, it is preferred to apply the minimum amount of coating composition. This level of add-on can be determined without undue experimentation for any particular fiber-coating system, and is usually within the range of 2 to 4 dry weight percent, by weight of the coated suture fiber.

To achieve specific desired properties, the coating compositions of this invention can further be plasticized by various agents such as glyceryl triacetate, butyl citrate, ethyl benzoate, dibutyl phthalate, etc. Various additives can also be included in the formulation to improve the performance of the lubricants such as calcium stearate or other salts of fatty acids, and bioabsorbable polyester and polyester-carbonate salts can be used. Also, water soluble lubricants such as a poly(alkylene oxide) can be included.

The coating composition can also include a poly(β -hydroxy butyrate-co- β -hydroxyvalerate) and/or a poly(β -hydroxybutyrate). A polymer of (β -hydroxybutyrate) can improve the knot run-down performance of a multifilament suture. Also, a polymer of (β -hydroxybutyrate) can be used as a binder, to hold the lubricant in place on the surface of a suture. Thus the lubricant can better resist displacement caused by friction during the knotting of the suture. Finally, tests indicate that poly(β -hydroxybutyrate-co- β -hydroxy valerate), and mixtures thereof, with calcium stearoyl-2-lactylate performs well under both suture dry and wet conditions.

The improvement in suture properties imparted to a synthetic bioabsorbable suture may be determined semiquantitatively by comparing the hand of a coated and uncoated suture during the act of tying down a single throw knot. Such a comparison can be made on both a wet and dry suture since many suture coatings show different tie-down properties when tested wet or dry. It is to be understood that the term wet tie-down refers to the testing of a coated suture in an in-vivo or in-vitro simulated fluid, and the ten day tie-down refers to bench top testing of a coated suture without exposure to an in-vivo or simulated fluid.

The method and the coating of the present invention are further illustrated by the following examples.

EXAMPLE 32

5 Into a heated polymerization reactor was charged 45g of glycolide, 55g of trimethylene carbonate (TMC), 9.23 mg of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$, and 97.21 of diethylene glycol (hereafter abbreviated as DEG). The reaction mixture was heated with stirring under dry nitrogen at 186°C for 75 minutes.

The resulting copolymer was discharged as a viscous melt which was cooled and ground to fine particles. The ground copolymer was dried under vacuum at 60°C overnight.

10 The copolymer had a composition of 47.7 weight percent trimethylene carbonate and 52.3 weight percent of glycolide. Less than 2.5 percent of monomeric trimethylene carbonate was present. The inherent viscosity was 0.98 dl/g.

EXAMPLE 33

15 The copolymer of Example 1 was formulated as follows for evaluation as a coating for a braided absorbable suture:

Coating Formulation 1 (Control)

6.0 grams of copolymer

9.0 grams of Xylene

20 80.0 grams of Methylene Chloride

Coating Formulation 2

6.0 grams of Calcium Stearoyl-2-Lactylate (Verv™)*

1.6 grams of copolymer

9.0 grams of Xylene

25 80.0 grams of Methylene Chloride

Coating Formulation 3

3.0 grams of Calcium Stearoyl Lactylate (Verv™)*

3.0 grams of Copolymer

4.5 grams of Xylene

30 40.2 grams of Methylene Chloride

EXAMPLE 34

35 A commercially available poly(β -hydroxybutyrate-co- β -hydroxyvalerate) was obtained from ICI Ltd., U.K. and then placed into the following formulations:

Coating Formulation 4 (Control)

0.45 grams of polymer

0.70 grams of Xylene

40 6.00 grams of Methylene Chloride

Coating Formulation 5

6.0 grams of Calcium Stearoyl -2-Lactylate (Verv™)*

1.6 grams of polymer

9.0 grams of Xylene

45 80.0 grams of Methylene Chloride

*C.J. Patterson Co., Kansas City, MO. U.S. A.

Five 20 foot lengths of size 2/0 polyglycolic acid braid was formed into five skeins. One skein was immersed in each of the formulations 1 to 5 above for 5 minutes. The skeins were then removed, allowed to drain, and dried for 1 hour. The dried skeins were then straightened and cut into suitable lengths.

50 Each length was then tied around a conventional tubular rubber tying board in the following manner. A single throw was made and then run down to the tubing to assess the resistance of the knot to rebound (the ability of the single throw to remain in position after the run down is complete). A square knot was then formed and run down to the tubing to assess the stick-slip of the knot (which is also termed chatter) as it runs down and to assess the force required to initiate and sustain the run down.

55 The rating system used to evaluate these coatings was:

Excellent - (a) No stick-slip during run down.

(b) Moderate force required which does not result in damage to the sleeve fibers of the suture.

(c) No rebound of the single throw.

- Good - (a) No stick-slip during run down.
 (b) Run-down force is a little high, but no damage is done to the sleeve fiber.
 (c) Minor rebound of the single throw.
- Fair - (a) Some stick-slip during run down.
 5 (b) Run-down force is somewhat high and minor damage to the sleeve fiber is noted.
 (c) Minor rebound of the single throw can occur.
- Poor - (a) High stick-slip in run down.
 (b) High damage or even breaking of the strand occurs.
 (c) High rebound of the single throw occurs.
- 10 The suture strands coated only with the glycolide/TMC copolymer of Formulation 1 were rated between Excellent and Good. The suture strands coated with the mixture of VervTM and the glycolide/TMC copolymer of Formulation 2 were rated Fair; the suture strands coated with the mixture of Formulation 3 were rated Excellent. The suture strands coated with Formulations 4 and 5 were both rated between Good and Excellent.

76

EXAMPLE 35

20 The commercially available poly(β -hydroxybutyrate-co- β -hydroxyvalerate) of Example 3, was formulated as follows.

- Coating Formulation 6
- 4.0 grams PHB-PHV 70/30 polymer
 4.0 grams of Calcium Stearyl Lactylate
 16.84 grams Xylene (19.6 cc)
 25 175.16 grams Methylene Chloride (133.1 cc)

All liquids are added to preweighed solids and the mixture is shaken for six hours at room temperature to get solubility.

A description of the coating method for the above suture and coating formulations is as follows. A commercially available coater (e.g. from the Bouligny Co., U.S.A.) is set to operate on a filament travelling 30 at a speed of 50 feet per minute. The circulating air in the drying oven is adjusted to be 80°C.

There is only one pass of the filament through the capillary coating apparatus, and then through the drying oven. The coating pump is adjusted to give about 5 to 8 drops per minute at the capillary apparatus.

Using the above coating method, the percent pick up was about 3.5 to 3.6 percent based on the weight of the filament. It is to be understood that this amount of pickup can be increased or decreased by any 35 person skilled in the art without undue experimentation by adjusting the above parameters. Preferably, the amount of pick up is increased by decreasing the amount of solvent in the formulation; and vice versa.

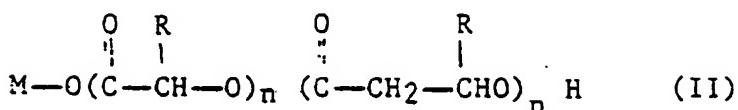
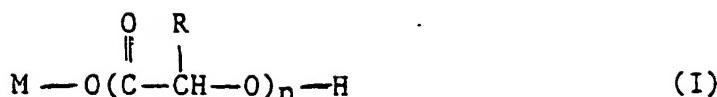
III

A random copolymer of glycolide and trimethylene carbonate containing less than sixty weight percent of glycolide is useful as a bioabsorbable coating material for a surgical suture and for surgical devices. A 40 multifilament synthetic absorbable suture coated with the bioabsorbable polymer of this invention exhibits knot run down performance that is superior and unexpected.

The random copolymer of this invention is amorphous and has a relatively low glass transition temperature. The random copolymer also has a relatively high molecular weight. The relatively high molecular weight enables the random copolymer to have reasonable tensile strength. The combined 45 chemical and physical properties prevent the copolymer from being brittle and easily flaking off the surface of a suture. Finally, the copolymer contains enough glycolide units to be bioabsorbable.

The random copolymer contains enough nonglycolide comonomer units to be readily soluble in common organic solvents. This solubility permits convenient coating from a solution of the polymer. Also, the copolymer contains enough glycolide units so it readily adheres to a glycolide-containing absorbable 50 braided suture.

The random polymer can be plasticized by various agents such as glyceryl triacetate, butyl citrate, ethyl benzoate, dibutyl phthalate, etc. Various additives can also be included in the formulation to improve the performance. Further, known lubricants can be included such as calcium stearate or other salts of fatty acids, calcium stearoyl lactylate, sodium stearoyl lactylate, a bioabsorbable polyester-carbonate salt, or a 55 bioabsorbable polyester salt such as:



10 wherein M is an alkali metal, for example sodium, an alkaline earth, for example calcium or magnesium, or hydrogen, or a combination of these. Finally, a water soluble lubricant such as poly(alkylene oxide)s can be added.

15 The random copolymer of this invention is not soluble in body fluids. The copolymer, therefore, will not be washed off by the first pass of a coated suture through tissue. Also, the copolymer can retain its lubricant properties while wet.

20 Poly(glycolide-co-trimethylene carbonate)s are bioabsorbable materials. They offer good biocompatibility and are specially useful as coatings or coating binders for bioabsorbable multifilament sutures. When used as coating materials, glycolide-trimethylene carbonate random copolymers improve the knot run-down performance of multifilament sutures. A 50% glycolide/50% TMC copolymer is a good coating material. The polymers can also be used as binders to hold lubricants in place on the surface of a suture in order to resist the displacement of the lubricant by friction during the knotting process.

25 The random copolymer of this invention can be prepared by the ring opening copolymerization of glycolide and trimethylene carbonate in the presence of a suitable catalyst, such as $\text{SnCl}_2 \bullet 2\text{H}_2\text{O}$, stannous octoate, zinc powder and the like. The polymerization is initiated by compounds containing one or more hydroxyl groups. The reaction is conducted with very pure and dry reactants, and under an inert gas atmosphere. The temperature of the reaction is sufficient to maintain the reaction mixture in a molten state until the polymerization is completed.

30 The random copolymer obtained is characterized by having an inherent viscosity of 0.5 to 3.0 dl/g as determined on a 0.5% solution of the polymer in hexafluoroacetone sesquihydrate at 30°C.

35 A 50% glycolide/50% trimethylene carbonate random copolymer has been evaluated as a coating material for a braided surgical suture containing essentially one hundred percent of glycolic acid ester linkages.

The random copolymer and the method of preparing the copolymer of this invention are described in the following examples.

35

EXAMPLE 36

40 Glycolide (5.5g), trimethylene carbonate (4.5g), 1.45 ml of a solution of $\text{SnCl}_2 \bullet 2\text{H}_2\text{O}$ in diethyl ether (conc. 0.429 mg/ml), and 0.216 ml of a solution of diethylene glycol in diethyl ether (conc. 1% v/v) were placed in a single neck 25 ml round-bottomed flask. After the diethyl ether was removed under reduced pressure, the flask was sealed with a stopcock and immersed in an oil bath heated at 180°C. The temperature of the oil bath was raised to 210°C in 55 minutes. Heating was continued at 210°C for another 145 minutes. The cooled polymerization product was removed from the flask and was dried under vacuum at 80°C overnight.

45 The copolymer had a glass transition temperature (T_g) of 9°C and was amorphous by DSC determination. The inherent viscosity was 1.24 dl/g. As determined by NMR, the product was a 59/41 (by weight) copolymer of glycolide and trimethylene carbonate. The residual trimethylene carbonate monomer level was around 2 weight percent.

50

EXAMPLE 37

55 Into a heated polymerization reactor was charged 45g of glycolide, 55g of trimethylene carbonate (TMC), 9.23 mg of $\text{SnCl}_2 \bullet 2\text{H}_2\text{O}$, and 97.2 μl of diethylene glycol (hereafter abbreviated as DEG). The reaction mixture was heated with stirring under dry nitrogen at 186°C for 75 min.

The resulting copolymer was discharged as a viscous melt which was cooled and ground to fine particles. The ground copolymer was dried under vacuum at 80°C overnight. The copolymer had a composition of 47.7 weight percent trimethylene carbonate and 52.3 weight percent of glycolide. Less than 2.5 percent of monomeric trimethylene carbonate was also present. The inherent viscosity was 0.98 dl/g.

5

EXAMPLE 38

- Glycolide (4.5g), trimethylene carbonate (5.5g), 1.62 ml of a solution of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ in diethyl ether (conc. 0.429 mg/ml), and 0.243 ml of a solution of diethylene glycol in diethyl ether (conc. 1% v/v) were placed in a single neck 25 ml round bottom flask. After the diethyl ether was removed under reduced pressure, the flask was sealed with a stopcock and immersed in an oil bath at 180°C. After 2 hours, the temperature was raised to 210°C. and heating was continued for an additional 1 hour. The cooled polymer was removed from the flask, ground in a mill, and dried under reduced pressure at 80°C. overnight. The final copolymer was a 47.4/52.6 (by weight) copolymer of glycolide and trimethylene carbonate. The Tg was 20°C. and the inherent viscosity was 1.46 dl/g.

20

To a 25 ml round-bottomed flask was charged 3.5g of glycolide, 6.5g of TMC, 1.62 ml of a solution of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ in diethyl ether (conc. 0.429 mg/ml), and 0.243 ml of a solution of diethylene glycol in diethyl ether (conc. 1% v/v). After the diethyl ether was removed under reduced pressure, the flask was sealed with a stopcock and heated at 165°C for one hour. Heating was then continued at 180°C for an additional 3 hours. The product was cooled, ground, and dried at 75°C under vacuum overnight. The copolymer was a 35/65 weight percent copolymer of glycolide and trimethylene carbonate. The residual trimethylene carbonate level was around 3 weight percent. The inherent viscosity was 1.85 dl/g and the glass transition temperature was -5.5°C as determined by DSC.

30

EXAMPLE 40

A 65.6/34.4 weight percent copolymer of glycolide and trimethylene carbonate was synthesized according to the procedure outlined in Example 2 except that the reaction temperature was 180°C. The ingredients and their quantity charged to the reactor were as follows:

Glycolide 72 g
 TMC 48 g
 $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ 7.4 mg
 DEG 0.0518 ml

40 The inherent viscosity of this material was 0.99 dl/g.

EXAMPLE 41

45 A 71.3/28.7 weight percent copolymer of glycolide and trimethylene carbonate was synthesized according to the procedure outlined in Example 2 except that the reaction temperature was 185°C. The ingredients and their quantity charged to the reactor were as follows:

Glycolide 80.4 g
 TMC 39.6 g
 $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ 7.3 mg
 DEG 0.0256 ml

50 The inherent viscosity of this product was 0.91 dl/g.

55

EXAMPLE 42

- A 74.3/25.7 weight percent copolymer of glycolide and trimethylene carbonate was prepared according to the procedure outlined in Example 4 except that the reaction temperature was 180°C. for 55 minutes, 5 and then was raised to 210°C. for 2 hours and 25 minutes. The ingredients and their quantity charged to the reactor were as follows:
- | | |
|---|---------|
| Glycolide | 98.5 g |
| TMC | 36.45 g |
| $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ | 8.17 mg |
| DEG in ether (1% v/v) | 2.86 ml |
- 10 The inherent viscosity of the copolymer was 1.07 dl/g.

EXAMPLE 43

- 15 To a round-bottomed flask was charged 7.5g of L-lactide, 2.5g of trimethylene carbonate, 3.62 ml of a solution of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ in diethyl ether (conc. 0.429 mg/ml) and 0.181 ml of a solution of diethylene glycol in diethyl ether (conc. 1% v/v). The polymerization was carried out according to the procedure outlined in Example 1. The product was an amorphous 74.6/25.4 copolymer of L-lactide and trimethylene carbonate 20 with an inherent viscosity of 0.81 dl/g and a glass transition temperature of 31°C.

The preferred coating polymer is approximately 50/50 (wt %) glycolide/trimethylene carbonate copolymer. Tests indicate that this copolymer and mixtures of the polymer with calcium salts such as calcium stearate or calcium stearoyl lactylate are promising coating materials for DEXON® braid. They perform well under both dry and wet conditions.

- 25 The method and the product of the present invention are further illustrated by the following examples. A 52.3/47.7 random glycolide/TMC copolymer of Example 2 was formulated as follows for evaluation as a coating for braided absorbable sutures.

Coating Formulation 7

- 30 6.0 grams of copolymer
9.0 grams of Xylene
80.0 grams of Methylene Chloride

Coating Formulation 8

- 6.0 grams of Calcium Stearoyl Lactylate (Verv™)*
1.6 grams of copolymer

- 35 9.0 grams of Xylene
80.0 grams of Methylene Chloride

Coating Formulation 9

- 3.0 grams of Calcium Stearoyl Lactylate (Verv™)*
3.0 grams of copolymer

- 40 4.5 grams of Xylene
40.2 grams of Methylene Chloride

*C. J. Patterson Co., Kansas City, MO, U. S. A.

A 20' length of size 2/0 polyglycolic acid braid was formed into a skein and immersed in each of these solutions for 5 minutes. The skeins were then removed, allowed to drain, and were dried for 1 hour. The 45 dried strands were then separated and cut into suitable lengths.

Each length was then tied around a conventional tubular rubber tying board as follows:

A single throw was made and then run down to the tubing to assess the resistance of the knot to rebound (the ability of the single throw to remain in position after the run-down is complete). A square knot was then formed and run down to the tubing to assess the stick-slip of the knot (chatter) as it runs 50 down and to assess the force required to initiate and sustain the run-down.

The rating system used to evaluate these coatings was:

- Excellent - (a) No stick-slip during run down.
 (b) Moderate force required which does not result in damage to the sleeve fibers of the suture.
 (c) No rebound of the single throw.
- Good - (a) No stick-slip during run-down.
 (b) Run-down force is a little high, but no damage is done to the sleeve fiber.
 (c) Minor rebound of the single throw.

Fair - (a) Some stick-slip during run down.

- (b) Run-down force is somewhat high and minor damage to the sleeve fiber is noted.

(c) Minor rebound of the single throw can occur.

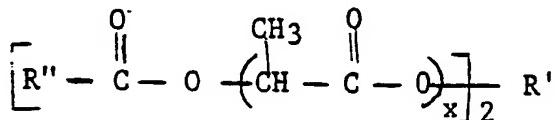
Difficult/Poor (a) High stick-slip in run down

- 5 (b) High damage or even breaking of the strand occurs.
(c) High rebound of the single throw occurs.

The suture strands coated only with the glycolide/TMC copolymer of Formulation 7 were rated between Excellent and Good. The suture strands coated with the mixture of Verv™ and the glycolide/TMC copolymer of Formulation 8 were rated Fair. The suture strands coated with the mixture of Verv™ and the glycolide/TMC copolymer of Formulation 9 were rated Excellent.

Claims

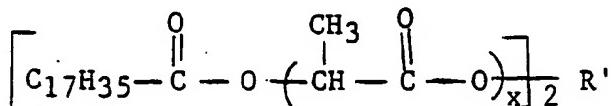
- 15 1. A surgical filament having a coating comprising a compound of the formula:



wherein x is at least 2, R' is selected from the group consisting of an alkaline-earth metal ion or radical, and R" is an alkyl group having at least 12 carbon atoms in the backbone.

- 25 2. A surgical filament having in combination a bioabsorbable suture or ligature and contained on the surface thereof a coating of claim 1 wherein Rⁿ is up to 22 carbon atoms.

3. A surgical filament of claim 2 wherein the suture or ligature is manufactured from a polymer containing at least one glycolic acid ester linkage, and the coating comprises a compound of the formula:



wherein x is at least 2 and R' is an alkaline-earth metal ion.

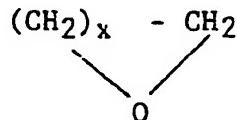
- 35 4. A surgical filament of claim 1 or 2 or 3 wherein x is at least 4 and/or R is an ion selected from the group consisting of magnesium, calcium, barium and zinc.

5. A bioabsorbable coating for a surgical suture or ligature comprising a block copolymer having one block characterized by one or more polyalkylene oxides.

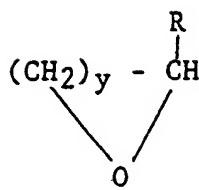
- 40 6. A bioabsorbable coating of claim 5 characterized by a diblock copolymer having a first block comprising a polyalkylene oxide and a second block consisting essentially of glycolic acid ester and trimethylene carbonate linkages.

7. A bioabsorbable coating of claim 5 characterized by a triblock copolymer having a middle block obtained by removing both terminal hydroxyl hydrogens from either a homopolymer of ethylene oxide, or from a block or random copolymer of ethylene oxide and a cyclic ether.

- 45 8. A bioabsorbable coating of claim 5 characterized by a triblock copolymer having a middle block obtained by removing both terminal hydroxyl hydrogens from a block or random copolymer of a first cyclic ether selected from the group consisting of



- 55 wherein x is 2 to about 9, and a second cyclic ether selected from the group consisting of



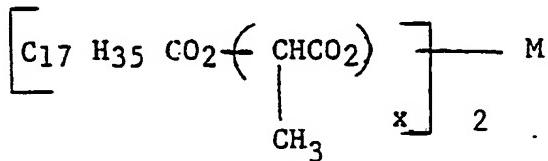
wherlein y is 1 to about 9 and R is a C₁ to C₈ alkyl group.

10 9. A surgical filament having a coating comprising a random copolymer having about 25 to 75 weight percent of glycolic acid ester linkages and the remaining linkages comprising at least trimethylene carbonate, said copolymer having a glass transition temperature at or below ambient temperature.

10. A surgical filament having a coating of claim 9 in combination with a lubricant additive of a stearoyl lactylate having the formula:

15

20



wherein X is at least two and M is an alkaline-earth metal ion.

25

30

35

40

45

50

55